Adult Immunization Update/ACIP Process

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Disclosures

- No financial conflict or interest with the manufacturer of any product named during this course.

Disclosures

- During this presentation I will discuss an off-label use for adolescent/adult tetanus-toxoid, reduced diphtheria-acellular pertussis vaccine (Tdap) as well as for human papillomavirus (HPV4 and HPV2), pneumococcal polysaccharide vaccine (PPSV23), and zoster vaccine

Overview

- 2014 adult schedule
- How ACIP makes its recommendations
- Pneumococcal vaccine recommendations
- Human papillomavirus vaccine
- Zoster vaccine

Recommended Adult Immunization Schedule—United States - 2014

Note: These recommendations must be read with the footnotes that follow containing number of doses, intervals between doses, and other important information.

Figure 1. Recommended adult immunization schedule, by vaccine and age group[1]

VACCINE ▼ / AGE GROUP ▶	19-21 years	22-26 years	27-49 years	50-59 years	60-64 years	≥ 65 years
Influenza[2,*]	1 dose annually					
Tetanus, diphtheria, pertussis (Td/Tdap)[3,*]	Substitute 1-time dose of Tdap for Td booster; then boost with Td every 10 yrs					
Varicella[4,*]	2 doses					
Human papillomavirus (HPV) Female[5,*]	3 doses					
Human papillomavirus (HPV) Male[5,*]	3 doses					
Zoster[6]					1 dose	
Measles, mumps, rubella (MMR)[7,*]	1 or 2 doses					
Pneumococcal 13-valent conjugate (PCV13)[8,*]	1 dose					
Pneumococcal polysaccharide (PPSV23)[9,10]	1 or 2 doses					1 dose
Meningococcal[11,*]	1 or more doses					
Hepatitis A[12,*]	2 doses					
Hepatitis B[13,*]	3 doses					
Haemophilus influenzae type b (Hib)[14,*]	1 or 3 doses					

*Covered by the Vaccine Injury Compensation Program

- For all persons in this category who meet the age requirements and who lack documentation of vaccination or have no evidence of previous infection; zoster vaccine recommended regardless of prior episode of zoster
- Recommended if some other risk factor is present (e.g., on the basis of medical, occupational, lifestyle, or other indication)
- No recommendation

Report all clinically significant postvaccination reactions to the Vaccine Adverse Event Reporting System (VAERS). Reporting forms and instructions on filing a VAERS report are available at www.vaers.hhs.gov or by telephone, 800-822-7967.

Information on how to file a Vaccine Injury Compensation Program claim is available at www.hrsa.gov/vaccinecompensation or by telephone, 800-338-2382. To file a claim for vaccine injury, contact the U.S. Court of Federal Claims, 717 Madison Place, N.W., Washington, D.C. 20005; telephone, 202-357-6400.

Additional information about the vaccines in this schedule, extent of available data, and contraindications for vaccination is also available at www.cdc.gov/vaccines or from the CDC-INFO Contact Center at 800-CDC-INFO (800-232-4636) in English and Spanish, 8:00 a.m. - 8:00 p.m. Eastern Time, Monday - Friday, excluding holidays.

Use of trade names and commercial sources is for identification only and does not imply endorsement by the U.S. Department of Health and Human Services.

The recommendations in this schedule were approved by the Centers for Disease Control and Prevention's (CDC) Advisory Committee on Immunization Practices (ACIP), the American Academy of Family Physicians (AAFP), the American College of Physicians (ACP), American College of Obstetricians and Gynecologists (ACOG) and American College of Nurse-Midwives (ACNM).

Figure 2. Vaccines that might be indicated for adults based on medical and other indications[1]

VACCINE ▼ / INDICATION ►	Pregnancy	Immuno-compromising conditions (excluding human immunodeficiency virus [HIV])[4,6,7,8,15]	HIV infection CD4+ T lymphocyte count[4,6,7,8,15]		Men who have sex with men (MSM)	Kidney failure, end-stage renal disease, receipt of hemodialysis	Heart disease, chronic lung disease, chronic alcoholism	Asplenia (including elective splenectomy and persistent complement component deficiencies)[8,14]	Chronic liver disease	Diabetes	Healthcare personnel
			< 200 cells/μL	≥ 200 cells/μL							
Influenza[2,*]	1 dose IIV annually				1 dose IIV or LAIV annually	1 dose IIV annually					1 dose IIV or LAIV annually
Tetanus, diphtheria, pertussis (Td/Tdap)[3,*]	1 dose Tdap each pregnancy	Substitute 1-time dose of Tdap for Td booster; then boost with Td every 10 yrs									
Varicella[4,*]	Contraindicated			2 doses							
Human papillomavirus (HPV) Female[5,*]		3 doses through age 26 yrs				3 doses through age 26 yrs					
Human papillomavirus (HPV) Male[5,*]		3 doses through age 26 yrs				3 doses through age 21 yrs					
Zoster[6]	Contraindicated			1 dose							
Measles, mumps, rubella (MMR)[7,*]	Contraindicated			1 or 2 doses							
Pneumococcal 13-valent conjugate (PCV13)[8,*]		1 dose									
Pneumococcal polysaccharide (PPSV23)[9,10]		1 or 2 doses									
Meningococcal[11,*]	1 or more doses										
Hepatitis A[12,*]	2 doses										
Hepatitis B[13,*]	3 doses										
Haemophilus influenzae type b (Hib)[14,*]		post-HSCT recipients only		1 or 3 doses							

*Covered by the Vaccine Injury Compensation Program

For all persons in this category who meet the age requirements and who lack documentation of vaccination or have no evidence of previous infection; zoster vaccine recommended regardless of prior episode of zoster

Recommended if some other risk factor is present (e.g., on the basis of medical, occupational, lifestyle, or other indications)

No recommendation

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

These schedules indicate the recommended age groups and medical indications for which administration of currently licensed vaccines is commonly indicated for adults ages 19 years and older, as of February 1, 2014. For all vaccines being recommended on the Adult Immunization Schedule: a vaccine series does not need to be restarted, regardless of the time that has elapsed between doses. Licensed combination vaccines may be used whenever any components of the combination are indicated and when the vaccine's other components are not contraindicated. For detailed recommendations on all vaccines, including those used primarily for travelers or that are issued during the year, consult the manufacturers' package inserts and the complete statements from the Advisory Committee on Immunization Practices (www.cdc.gov/vaccines/hcp/acip-recs/index.html). Use of trade names and commercial sources is for identification only and does not imply endorsement by the U.S. Department of Health and Human Services.

ACIP Meeting
Oct 23-24, 2013

- The recommendations to be discussed are primarily those of the Advisory Committee on Immunization Practices (ACIP)
  - composed of 15 non-government experts in clinical medicine and public health
  - provides guidance on use of vaccines and other biologic products to DHHS, CDC, and the U.S. Public Health Service

Timeline

- Public meetings – three times a year in Atlanta
- Concurrent teleconferences composed of Work Groups (WG) – meet bimonthly/monthly

Topics

- Determined Ad-hoc
- Four permanent WGs –
- Child/Adolescent
- Adult
- General Recommendations
- Influenza

Decisions

- Many issues reached by WG consensus
- Hot topics – ACIP discussion/vote
- 15 voting members, 31 liaisons, 8 ex-officios

Policy

- After ACIP vote decision shared with CDC director
- Director signs off – web site
- Placed in schedules – ACA coverage
- MMWR Publication – official CDC recommendation

Streptococcus pneumoniae

- Gram-positive bacteria
- 92 known serotypes
- Polysaccharide capsule important virulence factor
- No cross-protection

PCV13 Licensure

- PCV13 is approved by the Food and Drug Administration for:
  - children 6 weeks through 71 months of age
  - adults 50 years of age and older
- ACIP recommended use of PCV13 for immunocompromised persons 19 years and older (June 20, 2012)

Pneumococcal Polysaccharide Vaccine

- 60%-70% against invasive disease
- Less effective in preventing pneumococcal pneumonia

PCV13 and PPSV23 for High-Risk Adults 19 Years and Older*

- Administer a single dose of PCV13 to pneumococcal naïve adults with immunocompromising conditions including:
  - functional or anatomic asplenia, including sickle cell
  - chronic renal failure and nephrotic syndrome
  - CSF leak
  - cochlear implants
- Followed by a dose of PPSV23 at least 8 weeks later
- High risk adults who have previously received one or more doses of PPSV23, should receive a dose of PCV13 one or more years after the last PPSV23 dose was received

*ACIP off-label recommendation for PCV13 for adults 19 through 49 years of age

PPSV23 Second Dose for Adults 19 through 64 Years of Age

- Administer a second dose of PPSV23 at least 5 years after first dose of PPSV23 and at least 8 weeks after a dose of PCV13 to high-risk adults 19 through 64 years of age with:
  - functional or anatomic asplenia, including sickle cell disease
  - chronic renal failure or nephrotic syndrome
  - immunocompromising conditions including:
  - HIV, leukemia, lymphoma, Hodgkin's disease, multiple myeloma, generalized malignancy
  - immunosuppressive therapy (e.g., long-term systemic corticosteroids or radiation therapy)
  - organ or bone marrow transplant
- Does NOT apply to CSF leak or cochlear implant

PPSV23 for Adults
65 Years of Age and older

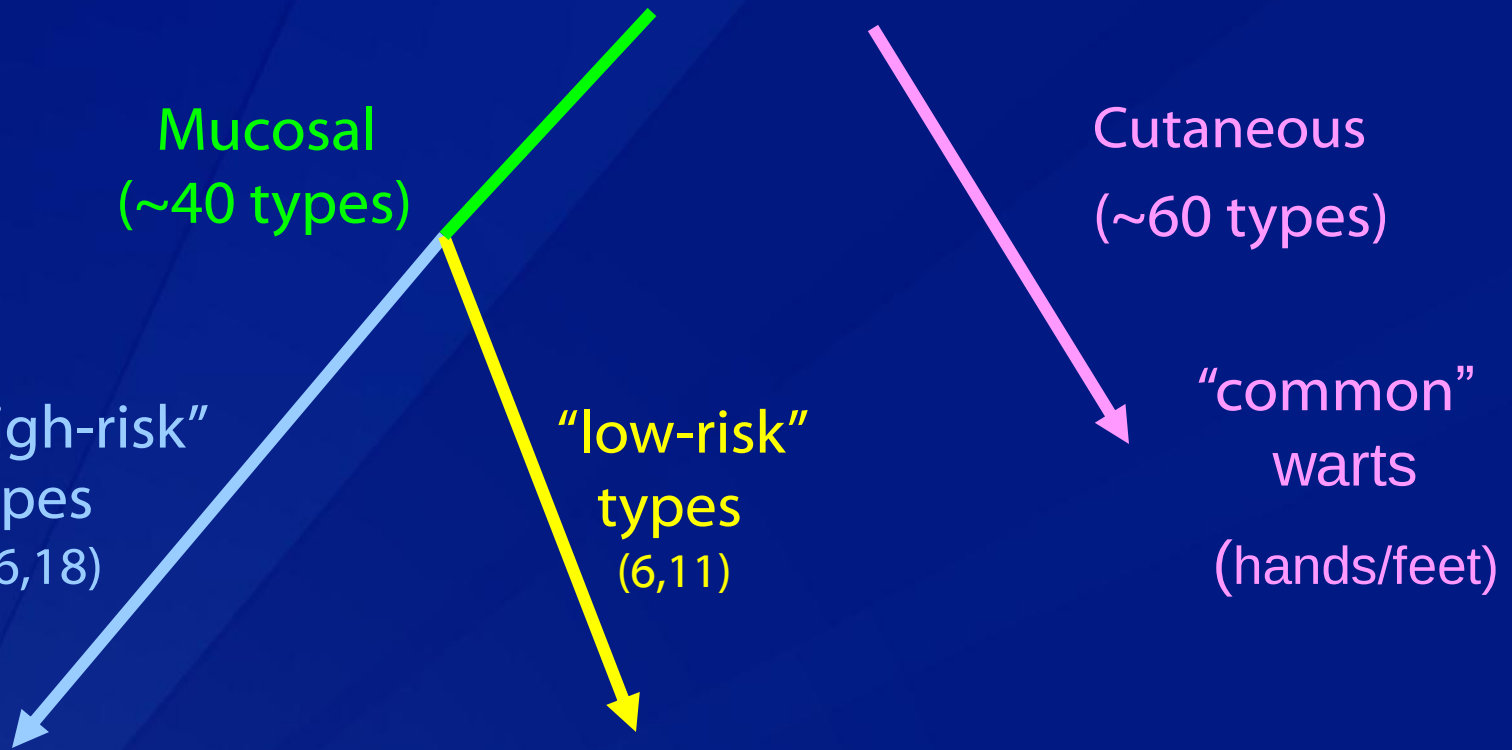
- Persons who received PPSV23 before age 65 years for any indication should receive another dose at age 65 or older if at least 5 years have passed since previous dose and 8 weeks since a dose of PCV13

- Those vaccinated with PPSV23 at or after age 65 do not need any additional doses

Administering PCV13 and PPSV23 Vaccines

- PCV13 and PPSV23 should not be administered simultaneously
- Administer PCV13 before PPSV23, whenever possible
- If PCV13 is administered first, wait 8 weeks to administer PPSV23
- If PPSV23 has already been administered, wait 1 year to administer PCV13

>100 HPV types



- low/high grade cervical abnormalities
- anogenital cancers

- low grade cervical abnormalities
- genital warts
- recurrent respiratory papillomas (RRP)

HPV Infection

- Almost females and males will be infected with at least one type of HPV at some point in their lives
  - Estimated 79 million Americans currently infected
  - 14 million new infections/year in the US
  - HPV infection is most common in people in their teens and early 20s
- Most people will never know that they have been infected

Jemal A et al. J Natl Cancer Inst 2013;105:175-201

Cervical Cancer

- Cervical cancer is the most common HPV-associated cancer among women
  - 500,000+ new cases and 275,000 attributable deaths world-wide in 2008
  - 12,000+ new cases and 4,000 attributable deaths in 2011 in the U.S.
- 25.9% cervical cancers occur in women who are between the ages of 35 and 44
  - 14% between 20 and 34
  - 23.9% between 45 and 54

HPV Vaccine

Quadrivalent/HPV4 (Gardasil)	Name	Bivalent/HPV2 (Cervarix)
Merck	**Manufacturer**	GlaxoSmithKline
6, 11, 16, 18	**Types**	16, 18
Females: Anal, cervical, vaginal and vulvar precancer and cancer; Genital warts **Males:** Anal precancer and cancer; Genital warts	**Indications**	**Females:** Cervical precancer and cancer **Males:** Not approved for use in males
Pregnancy Hypersensitivity to yeast	**Contraindications**	Pregnancy Hypersensitivity to latex (latex only contained in pre-filled syringes, not single-dose vials)
3 dose series: 0, 2, 6 months	**Schedule (IM)**	3 dose series: 0, 1, 6 months

HPV Vaccines

- Clinical trials using cancer as the end-point would take many years to complete
- Both manufacturers used established cervical cancer precursors as the end-point
  - cervical intraepithelial neoplasia (CIN)
  - adenocarcinoma in-situ

HPV Vaccine Efficacy

	HPV4 16-26 y/o females		HPV2 15-25 y/o females	
	N	VE	N	VE
HPV 16/18 CIN2/3 or AIS	8,493	98%	7,344	93%
HPV 6/11 EGL	6,932	99%	--	--

Vaccine Efficacy for HPV 6,11,16,18-Related External Genital Lesions (EGL) for Boys and Men 16 Through 26 Years of Age

Endpoint	Vaccine Group (N=1397)	Placebo Group (N=1408)	Efficacy (%)
HPV 6/11/16/18-related EGL	3	31	90
HPV 6/11/16/18-related condyloma	3	28	89
HPV 6/11/16/18-related PIN* 1/2/3	0	3	100*

HPV Vaccine Recommendations

Females:

Administer to females ages 11 through 26 years if not previously vaccinated

Males:

Administer 11 through 21 years of age if not previously vaccinated

Administer 22 through 26 years of age if HIV-positive, immunosuppressed or MSM

HPV4 may be administered to males 22 through 26 years of age

HPV Vaccine Recommendations

- Routine: 3 –dose series to females 11- 26 years
- May be given to females 9-10 years
- HPV4 *may be administered* in a 3-dose series to males aged 9 through 26 years to reduce their likelihood of acquiring genital warts
- HPV2 not approved for males of any age or for the prevention of genital warts

MMWR 2010;59(No. 20):630-2

HPV Vaccine "Special Situations"

- Vaccine can be administered to females with:
  - equivocal or abnormal Pap test
  - positive HPV DNA test
  - genital warts
  - immunosuppression
  - Breastfeeding

MMWR 2010: 59(No. 20);626-9

HPV Vaccination Schedule

- Routine schedule is 0, 1-2, 6 months
- Minimum intervals
  - 4 weeks between doses 1 and 2
  - 12 weeks between doses 2 and 3
  - 24 weeks between doses 1 and 3

HPV Vaccine Intervals

- There is no MAXIMUM interval between HPV vaccine doses
- If the interval between doses is longer than recommended the series should be continued where it was interrupted
  - do not repeat the series or add doses

HPV Vaccine Safety Data Sources

- Post-licensure safety data (VAERS)[1]
- Post-licensure observational comparative studies (VSD)[2]
- Ongoing monitoring by CDC and FDA
- Post-licensure commitments from manufacturers
  - Vaccine in pregnancy registries
  - Long term follow-up in Nordic countries
- Official reviews
  - WHO's Global Advisory Committee on Vaccine Safety [3]
  - Institute of Medicine's report on adverse effects and vaccines, 2011[4]

[1]Vaccine Adverse Events Reporting System, http://vaers.hhs.gov/index
[2]Vaccine Safety Datalink, http://www.cdc.gov/vaccinesafety/Activities/VSD.html
[3]http://www.who.int/vaccine_safety/Jun_2009/en/
[4]http://www.iom.edu/Reports/2011/Adverse-Effects-of-Vaccines-Evidence-and-Causality.aspx

HPV Vaccine Impact: HPV Prevalence Studies

- NHANES Study
  - National Health and Nutrition Examination Survey (NHANES) data used to compare HPV prevalence before the start of the HPV vaccination program with prevalence from the first four years after vaccine introduction
  - In 14-19 year olds, vaccine-type HPV prevalence decreased 56 percent, from 11.5 percent in 2003-2006 to 5.1 percent in 2007-2010
  - Other age groups did not show a statistically significant difference over time
  - The research showed that vaccine effectiveness for prevention of infection was an estimated 82 percent

Cummings T, Zimet GD, Brown D, et al. Reduction of HPV infections through vaccination among at-risk urban adolescents. Vaccine. 2012; 30:5496-5499.

HPV Vaccine Impact: HPV Prevalence Studies, continued

- Clinic-Based Studies
  - Significant decrease from 24.0% to 5.3% in HPV vaccine type prevalence in at-risk sexually active females 14-17 years of age attending 3 urban primary care clinics from 1999-2005, compared to a similar group of women who attended the same 3 clinics in 2010

Kahn JA, Brown DR, Ding L, et al. Vaccine-Type Human Papillomavirus and Evidence of Herd Protection After Vaccine Introduction. Pediatrics. 2012; 130:249-56.

HPV Vaccine Impact: Genital Warts Studies

- Ecologic analysis used health claims data to examine trends in anogenital warts from 2003-2010 among a large group of private health insurance enrollees
  - The study found significant declines after 2007 in females aged 15-19 year (38% decrease from 2.9/1000 PY in 2006 to 1.8/1000 PY in 2010)
  - Smaller declines were observed among those 21-30 years but not in those over 30 years
- A similar study evaluated genital wart trends in males and females attending public family planning clinics and found
  - Significant decrease of 35% in females under 21 years of age and a 19% decrease in males less than 21 years
  - No decreases were reported in the older males or females

HPV Vaccine Impact:
High HPV Vaccine Coverage in Australia

- 80% of school-age girls in Australia are fully vaccinated
- High-grade cervical lesions have declined in women less than 18 years of age
- For vaccine-eligible females, the proportion of genital warts cases declined dramatically by 93%
- Genital warts have declined by 82% among males of the same age, indicating herd immunity

Garland et al, Prev Med 2011
Ali et al, BMJ 2013

Tips and Time-savers for Talking with Parents about HPV Vaccine

Recommend the HPV vaccine series the same way you recommend the other adolescent vaccines. For example, you can say "Your child needs these shots today," and name all of the vaccines recommended for the child's age.

Parents may be interested in vaccinating, yet still have questions. Taking the time to listen to parents' questions helps you save time and give an effective response. CDC research shows these straightforward messages work with parents when discussing HPV vaccine—and are easy for you or your staff to deliver.

CDC RESEARCH SHOWS: The "HPV vaccine is cancer prevention" message resonates strongly with parents. In addition, studies show that a strong recommendation from you is the single best predictor of vaccination.

TRY SAYING: HPV vaccine is very important because it prevents cancer. I want your child to be protected from cancer. That's why I'm recommending that your daughter/son receive the first dose of HPV vaccine today.

CDC RESEARCH SHOWS: Disease prevalence is not understood, and parents are unclear about what the vaccine actually protects against.

TRY SAYING: HPV can cause cancers of the cervix, vagina, and vulva in women, cancer of the penis in men, and cancers of the anus and the mouth or throat in both women and men. There are about 26,000 of these cancers each year—and most could be prevented with HPV vaccine. There are also many more precancerous conditions requiring treatment that can have lasting effects.

CDC RESEARCH SHOWS: Parents want a concrete reason to understand the recommendation that 11–12 year olds receive HPV vaccine.

TRY SAYING: We're vaccinating today so your child will have the best protection possible long before the start of any kind of sexual activity. We vaccinate people well before they are exposed to an infection, as is the case with measles and the other recommended childhood vaccines. Similarly, we want to vaccinate children well before they get exposed to HPV.

CDC RESEARCH SHOWS: Parents may be concerned that vaccinating may be perceived by the child as permission to have sex.

TRY SAYING: Research has shown that getting the HPV vaccine does not make kids more likely to be sexually active or start having sex at a younger age.

CDC RESEARCH SHOWS: Parents might believe their child won't be exposed to HPV because they aren't sexually active or may not be for a long time.

TRY SAYING: HPV is so common that almost everyone will be infected at some point. It is estimated that 79 million Americans are currently infected with

An anti-cancer vaccine

- The "HPV vaccine is cancer prevention" message resonates strongly with parents
  - In focus groups and online panels, mothers wanted more information on the types of HPV cancers
  - In focus groups mothers stated they were influenced to vaccinate their child because HPV vaccine prevents cancer, they had a family history of cervical cancers, and/or because they had a personal experience with cervical cancer

Zoster: Complications

- Post-herpetic neuralgia
- Pain that lasts after rash clears, sometime up to a year
- Occurs in 20 percent of shingles cases
- Highest risk in persons older than 60 years

Herpes Zoster Vaccine Efficacy

- Pre-licensure:
- 36,716 persons 60+ years of age followed for 3 years after vaccination
- 51.3% fewer episodes of HZ
- 66.5% less postherpetic neuralgia

Zoster Vaccine

- Recommended for persons 60 years old and older
- Indicated for persons with current varicella immunity based on disease
- Indicated regardless of a history of zoster
- One dose, 0.6 cc subcutaneous injection

Zoster Vaccine: Post-licensure Efficacy

- Zoster Efficacy and Safety Trial (ZEST)
- 22,400 50-59 year olds
- 70% effective in prevention of zoster

Zoster Vaccine

- Now licensed for adults 50-59 years of age
- Routine vaccination of adults younger than 60 years NOT recommended
- Reduced supply
- Burden of complications highest in persons older than 60 years

Zoster Vaccine Criteria of Varicella Immunity

1. Laboratory evidence of immunity or laboratory confirmation of disease
2. Born in U.S. before 1980*
3. Health-care provider diagnosis of or verification of varicella disease
4. Health-care provider diagnosis of zoster

- *Does not apply to health-care providers, immunosuppressed, or pregnant

Zoster Vaccine

- Screening for a history of varicella disease is not necessary or recommended
- Persons 60 years of age and older can be assumed to be immune regardless of their recollection of chickenpox (so don't ask)

Zoster Vaccine

- If tested and seronegative - 2 doses of single antigen varicella vaccine (Varivax®) separated by at least 4 weeks
- Zoster vaccine – not indicated for persons with immunity due to vaccine

Thank You

- **CDC-Info web site: www.cdc.gov/info**
- **Email: nipinfo@cdc.gov**
- **Web site: www.cdc.gov/vaccines**